

# Cefepime neurotoxicity can mimic postanoxic coma with myoclonic status epilepticus

Sara Hocker, MD

Alejandro A. Rabinstein, MD

**A** 61-year-old woman admitted for operative treatment of aortic and mitral stenosis and coronary artery bypass grafting developed encephalopathy and abnormal movements postoperatively. The evening after surgery, she was hypoxic and hypotensive. The following day, she was awake and following commands without any obvious focal deficits. Over subsequent days her mental status worsened as she remained in shock. Hypoperfusion of the kidneys and liver resulted in acute tubular necrosis and transaminitis. On postoperative day 2 she was started empirically on cefepime and vancomycin for fever and leukocytosis of unknown origin. Her level of consciousness gradually declined and by the fifth postoperative day she was comatose and had developed repetitive involuntary movements of the face consisting of sudden opening of the eyes and opening and closing of the jaw. The movements of the mouth were forceful enough to damage 2 endotracheal tubes. She also had dystonic-like movements in the lower extremities. The movements had myoclonic features but at times appeared more dystonic and were strongly exacerbated by stimulation, particularly when applied to the feet (video). Dexmedetomidine was used to minimize the movements. When sedation was held the movements increased and her examination otherwise remained unchanged. The patient's eyes were partially open but she did not track light or moving objects. Brainstem reflexes were preserved but she had no motor response to pain in any of the extremities. A noncontrast CT scan of the brain showed no intracranial pathology. An EEG showed no electroencephalographic correlate to the movements. The background was diffusely slow in the range of 1–4 Hz with intermixed  $\theta$  and  $\beta$  activity and no reactivity was observed. The following day, the patient's antibiotic regimen was changed from cefepime to piperacillin/tazobactam for additional anaerobic coverage as fever and leukocytosis remained present and no source had been identified. On the sixth postoperative day, she had regained consciousness and could interact with family and examiners. She could answer questions by shaking and nodding her head and could follow commands in all extremities. The abnormal movements were much less prominent and did not require dexmedetomidine to prevent damage to the endotracheal tube; however, the presence of the tube clearly made the movements of the face more frequent. The following day she underwent tracheostomy placement with removal of the endotracheal tube after which the facial movements disappeared.

Supplemental Data

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Department of Neurology, Mayo Clinic, Rochester, Minnesota.

Correspondence to: [hocker.sara@mayo.edu](mailto:hocker.sara@mayo.edu)

## DISCUSSION

On the day of our initial evaluation there was concern for anoxic-ischemic brain injury resulting from her tenuous hemodynamic status including multiple episodes of hypotension and hypoxia over the preceding 5 days since her surgery. Factors that prompted concern for anoxic-ischemic injury included 1) the presence of coma and movements resembling myoclonic status epilepticus, 2) the history of cardiac surgery complicated by multiple episodes of hypoxia and hypotension, and 3) the lack of normal reactivity on EEG.

Semiologically, the movements were suggestive of myoclonus with dystonic features. This categorization was supported by their triggering and exacerbation with external stimulation and lack of correlation with ventilation cycles. While the movements did not have the bilateral asymmetric and asynchronous myoclonic jerks typically seen with myoclonic status epilepticus, the myoclonic appearance, stimulus sensitivity, and intensity of the movements were similar, and given the clinical context, could mimic myoclonic status epilepticus.

The lack of evidence of structural brain damage on CT scan, as well as the superimposed infection and renal and liver insufficiency, led us to be cautious with prognostication. There was remarkable improvement in her condition only 24 hours after discontinuation of cefepime without any other major changes in her clinical situation.

Cefepime neurotoxicity typically manifests as encephalopathy with or without myoclonus, seizures, or nonconvulsive status epilepticus.<sup>1,2</sup> The mechanism of seizure generation has been shown to be due to the drug-induced suppression of inhibitory neurotransmission via a concentration-dependent modulation of the  $\gamma$ -aminobutyric acid receptors.<sup>3</sup>

Renal insufficiency is a well-recognized risk factor for cefepime neurotoxicity<sup>4,5</sup> and it was present in our patient; however, cases of encephalopathy and status epilepticus have been reported in patients with normal renal function.<sup>6,7</sup>

Cefepime neurotoxicity is not widely recognized by clinicians. There is typically a delay of 3 to 5 days between onset of symptoms and diagnosis, as illustrated by our patient.<sup>2</sup> If consulted for encephalopathy or coma, the clinician should consider cefepime as a possible culprit when reviewing the medication list. In those patients who are receiving cefepime, an EEG is indicated to rule out nonconvulsive SE. Coma leading to death has been observed in some cases<sup>1,5</sup> and, indeed, our patient's presentation mimicked coma with myoclonic status epilepticus after anoxic-ischemic insult. If asked to provide neurologic prognostication in a comatose patient receiving cefepime, this antibiotic should be discontinued and a period of time should be allowed to elapse before prognostication is attempted.

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## DISCLOSURES

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